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A new approach to estimate aerobic fitness using the NHANES dataset

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Abstract

Introduction: Physical activity and fitness are essential for healthy growth in children. The National Health and Nutrition Examination Survey (NHANES) evaluated fitness by estimating $\dot{V}O_2$max from submaximal measurements of heart rate (HR) during graded treadmill exercise. Our aims were (a) to examine how well NHANES methodology used to *estimate* $\dot{V}O_2$max correlated with *actual* VO_2max and (b) to evaluate a novel fitness metric using actual data collected during exercise and its relationship to physical activity and sedentary time, lipid profiles, and body composition.

Methods: Fifty-three adolescents completed NHANES submaximal exercise protocol and maximal graded cardiopulmonary exercise testing. We used a novel approach to quantifying fitness (Δvelocity × incline × body mass (VIM)/ΔHR slopes) and evaluated its relationship to physical activity and sedentary time using NHANES data (n = 4498). In a subset (n = 740), we compared ΔVIM/ΔHR slopes to NHANES estimated $\dot{V}O_2$max and examined their relationship to cardiovascular risk factors (BMI percentiles and lipid levels).

Results: Measured $\dot{V}O_2$peak was moderately correlated with NHANES estimated $\dot{V}O_2$max (r = 0.53, $P < 0.01$). Significantly higher ΔVIM/ΔHR slopes were associated with increased physical activity and decreased sedentary time. ΔVIM/ΔHR slopes were negatively associated with LDL, triglycerides, and BMI percentiles ($P < 0.01$). In general, the two fitness models were similar; however, ΔVIM/ΔHR was more discriminating than NHANES in quantifying the relationship between fitness and LDL levels.

Conclusion: We found that the NHANES estimated $\dot{V}O_2$max accounted for approximately 28% of the variability in the measured $\dot{V}O_2$peak. Our approach to estimating fitness (ΔVIM/ΔHR slopes) using actual data provided similar relationships to lipid levels. We suggest that fitness

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CONFLICT OF INTEREST
The authors declare no conflicts of interest. The results of the present study do not constitute endorsement by ACSM. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

SUPPORTING INFORMATION
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measurements based on actually measured data may produce more accurate assessments of fitness and, ultimately, better approaches linking exercise to health in children.

Keywords

adolescents; cardiorespiratory fitness; children; exercise

1 | INTRODUCTION

The objective of this study was to test a novel analytic approach for quantifying physical fitness in pediatric populations. New approaches are needed for several reasons. First, physical fitness in children tracks across the life span[1-3] and plays a mechanistic role in the diagnosis, therapy, and prevention of both pediatric and adult diseases.[4-6] For example, higher levels of fitness in children and young adults are associated with lower cardiovascular disease risk and mortality.[7] Despite this, common approaches to cardiopulmonary exercise testing (CPET) in children do not yet exist.[8] Second, although peak or maximal oxygen uptake ($\dot{V}O_2$max) is the predominant biomarker of physical fitness in children and adults, its measurement requires elaborate CPET equipment and personnel. These factors have limited the feasibility of laboratory CPET to quantify physical fitness in large population and/or field-based studies.

Consequently, in many cases, $\dot{V}O_2$max is estimated from submaximal exercise tests or field tests. The actual data collected [typically, minutes or seconds from a mile run; or number of laps completed in the 20-m shuttle[9,10]] are used in complex algorithms to calculate $\dot{V}O_2$max. The algorithms often include subjective data on the participant's level of habitual physical activity or normative values obtained from studies in adults. Such approaches can confound data interpretation due to misspecification, collinearity, inappropriate reference values, and mathematical coupling.[11-14] As noted in a recent review of pediatric CPET by Pianosi and coworkers,[15] in contrast to peak $\dot{V}O_2$ actually measured in CPET, peak $\dot{V}O_2$ estimates derived from submaximal tests "are characterized by large variability, and therefore less reliability, validity, and robustness".

In this research, we examined the protocols and predictive equations used to gauge fitness in the National Health and Nutrition Examination Survey (NHANES) study in adolescents, one of the largest datasets of physical fitness collected in youth.[16] The NHANES method has not been validated in adolescents to our knowledge. As highlighted below and shown in Figure 1A, the NHANES *estimated* $\dot{V}O_2$max is calculated from a series of variables ranging from actually measured heart rate (HR) to survey recall approximations of habitual physical activity (including prediction equations derived from primarily middle-aged men). The directly measured HR, as well as predicted values for $\dot{V}O_2$, is determined in large measure by the participant's work rate, and in treadmill exercise, work rate is a direct function of treadmill velocity and incline. The first aim of our study was to examine the criterion validity of the NHANES estimated $\dot{V}O_2$max methodology by comparing the NHANES estimated $\dot{V}O_2$max (NHANES submaximal protocol) with *actual* VO_2max in a current study sample of adolescents. The second aim of our study was to evaluate a novel fitness metric (VIMHR fitness biomarker) using actual data collected during exercise and its relationship to key moderators and mediators of physical fitness such as body mass, habitual physical activity and sedentary time, and circulating lipid levels. To accomplish this aim, we reanalyzed existing NHANES data from 4498 participants using an approach to calculating work rate on a treadmill described by Bar-Yoseph et al[17] We hypothesized that useful biomarkers of fitness in the NHANES cohort of adolescents could be simplified by relying on actually measured variables, namely HR, body mass, and treadmill velocity and incline (VIM-HR fitness biomarker; Figure 1B). By using the available data, our approach to fitness would minimize assumptions and possible errors compared to traditional estimates of $\dot{V}O_2$ max and help avoid some of the possible confounding effects.

2 | METHODS

2.1 | Current study sample (UCI PERC)

2.1.1 | Visit 1: Baseline data, cardiopulmonary exercise testing, and body composition—This study was approved by the institutional review board at the University of California, Irvine (UCI), and informed consent and assent were obtained from all participants and their legal guardians. Fifty-three healthy 12- to 18-year-old adolescents participated in the age range that matched the NHANES cohort. The study consisted of two separate visits to the UCI Pediatric Exercise and Genomics Research Center (PERC) laboratory.

Anthropometric measurement and body composition: Standard calibrated scales and stadiometers were used to determine weight and height. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Sex-specific BMI percentile-for-age and BMI categories were calculated.[18]

Cardiopulmonary exercise testing: The participants performed a standardized maximal progressive intensity protocol on a treadmill in which velocity and incline increased throughout the test. Gas exchange was measured breath-by-breath, and HR was measured continuously. The increase in treadmill velocity and incline was designed to achieve as linear a $\dot{V}O_2$ response to exercise as possible.[17] Peak $\dot{V}O_2$ was calculated as the 20-second rolling averages of the highest value over the last 2 minutes of progressive exercise. We used respiratory exchange ratio ≥ 1.0 to corroborate that the participant exercised at or close to maximal exercise.[19]

2.1.2 | Visit 2: NHANES Submaximal exercise protocol—We followed the NHANES submaximal exercise testing protocol to determine the NHANES estimated $\dot{V}O_2$ max/kg. Schematics of two approaches to measuring $\dot{V}O_2$max (direct measurement and NHANES estimated) are shown in Figure 1A,B. The NHANES fitness variable, $\dot{V}O_2$max/body weight, is expressed in units of milliliter O_2 per minute per kilogram. Gas exchange was not measured in the NHANES dataset. Instead, participants performed a submaximal treadmill exercise protocol and the investigators used HR data obtained at two different work intensities (stages 1 and 2) to estimate $\dot{V}O_2$max. In our analyses, we included HR and gas exchange at warm-up and at stages 1 and 2 to use as much of the available data.

NHANES Submaximal exercise testing protocol: determination of treadmill velocity and incline: In order to determine an appropriate treadmill velocity and incline for the stages, the NHANES protocol first calculated a *predicted* $\dot{V}O_2$max for each participant using a prediction formula[20] that used age (years), weight, height, sex, and an estimate of habitual physical activity, physical activity readiness (PAR).

Predicted $\dot{V}O_2$max (ml/min/kg) = 56.363 + (1.921 × PAR) − (0.381 × Age) − (0.754 × BMI) + (10.987 × Sex).

Sex was determined as male = 1 and female = 0. The PAR was based on a physical activity recall questionnaire (scores ranging from 0 to 7). Based on the participant's calculated predicted $\dot{V}O_2$max, he or she was assigned to 1 of 8 treadmill test protocols that specified treadmill velocity, incline, and duration for a warm-up (2 minutes) and stages 1 and 2 (3 minutes each). For participants, 12-18 years old, the predicted protocol was subtracted by 2 to get the assigned protocol for this age-group; protocols 1, 2, and 8 were excluded in this age-group. The stages were selected to achieve $\dot{V}O_2$ (had it been measured) equal to 45% (warm-up), 55% (stage 1), and 75% (stage 2) of maximal values. The selection of velocity and incline for the stages is a critical determinant of the NHANES fitness calculation, because the *estimated* value of $\dot{V}O_2$ at each stage was used along with the *measured* value of HR to ultimately estimate $\dot{V}O_2$max (Figure 1A). HR data were recorded at the end of warm-up and at each exercise stage.

NHANES Calculation of estimated $\dot{V}O_2$max: As shown in Figure 1A, the NHANES estimated $\dot{V}O_2$max (ml/min/kg body weight) is based on three key assumptions:

- HR and $\dot{V}O_2$ are linearly related during progressive exercise.
- The relationship of HR and $\dot{V}O_2$, when $\dot{V}O_2$ is normalized to body weight, is independent of body size.
- Maximal HR (HRmax) can be accurately estimated using the following equation:

$$\mathrm{HR\ max} = 220 - \mathrm{age}$$

The linear relation between $\dot{V}O_2$ and HR during exercise is given by:

$$\mathrm{HR} = (\Delta \mathrm{HR} / \Delta \dot{V}O_2) \times \dot{V}O_2 + b$$

in which $\Delta HR/\Delta \dot{V}O_2$ is the slope and b is the y-intercept. The estimate of $\dot{V}O_2$max is given by:

$$\text{HR max} = (\Delta\text{HR} / \Delta\dot{V}O_2) \times \dot{V}O_2\,\text{max} + b, \text{and}$$

$$\dot{V}O_2\,\text{max} = \frac{\text{HRmax} - b}{\Delta\text{HR} / \Delta\dot{V}O_2}$$

To calculate the slope, NHANES used the following:

$$\text{Slope} = \frac{\text{measured HR}_{\text{stage 2}} - \text{measured HR}_{\text{stage 1}}}{\text{estimated }\dot{V}O_{2\text{stage 2}} - \text{estimated }\dot{V}O_{2\text{stage 1}}}$$

To calculate b (the y-intercept), the NHANES used the midpoint of the measured stage 1 and 2 HR values and the midpoint of the stage 1 and 2 estimated $\dot{V}O_2$ values as follows:

$$b = [(\text{measured HR}_{\text{stage 1}} + \text{measured HR}_{\text{stage 2}}) / 2] - \text{Slope} \times [(\text{estimated }\dot{V}O_{2\text{stage 1}} + \text{estimated }\dot{V}O_{2\text{stage 2}}) / 2]$$

2.2 | Analysis of existing NHANES data using a novel approach

2.2.1 | NHANES Sample—NHANES fitness data, including the measured and estimated variables needed to calculate $\dot{V}O_2$max, are available to the public.[16] The study protocols were approved by the National Health Statistics institutional review board. All NHANES participants (or their parents/guardians) gave written informed consent. We retrospectively analyzed fitness data from NHANES datasets 1999-2000, 2001-2002, and 2003-2004. The NHANES treadmill exercise protocol was completed in 4508 participants 12 years and older (mean age 15 ± SD 2, 51% male). We included participants who had complete data on body composition and cardiorespiratory fitness testing (n = 4498). Underweight participants (BMI percentile < 5th percentile) were excluded from analyses as they were too few in number (n = 135).

2.2.2 | Physical activity and sedentary time variables—Self-recall physical activity variables were dichotomized into "yes" or "no" for activities performed during the 30 days prior to the exercise test (adapted from Pate et al[21]). Additionally, participants were asked if they thought that their amount of activity during the past 30 days was more, less, or about the same as that of others of the same age and sex. Sedentary activity questions differed by age-group. Participants aged 16-19 years reported the amount of time on a typical day during the past 30 days that they spent sitting and watching television or videos or using a computer outside of work. Children aged 12-15 years were asked about the previous day's television viewing and computer use/computer games separately. The two questions were summed and categorized as either ≤ or >2 hours per day, based on previous recommendations.[22]

2.2.3 | NHANES lipid screening—We analyzed lipid levels for participants in the 2003-2004 cohort (n = 740), including total serum cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL).[23]

2.2.4 | An alternative approach to estimating fitness from the NHANES dataset—As can be seen in the above description, converting submaximal HR data to an estimate of $\dot{V}O_2max$ is complex (Figure 1A). In the case of adolescents, the NHANES approach requires substantial data obtained from participants that differed profoundly in age and sex.[20] As noted earlier, we employed a strategy developed by Bar-Yoseph et al[17] that minimizes assumptions and gauges fitness by relating the physiological output variable (in this case, HR) to as accurate as possible quantification of the driving input. We aimed to use the NHANES actual data to quantify fitness, namely body weight and HR measured at stages of treadmill exercise, in which the velocity and incline were precisely known. Relying on the fundamental principle that work is a function of mass × velocity[2], work rate (we refer to as VIM) done during treadmill exercise can be calculated from the treadmill velocity (V), incline (I), and the body mass (M) of each participant using the following equation:

$$\mathrm{VIM} = V^2 \times (I + 1) \times M$$

Treadmill incline is typically expressed as degrees or percent. Consequently, we substituted $(I + 1)$ for I since otherwise the work performed at 0% incline would calculate as zero. In previous work, we found that VIM in treadmill CPET is highly correlated with work rate in cycle ergometer CPET (work rate is directly measured in cycle ergometers).[17] Using VIM in lieu of work rate for treadmill exercise, we found expected relationships among CPET variables, body mass, and additional gas exchange biomarkers of the systemic physiological responses to exercise.

The alternative fitness biomarker was then determined as the slope of the relationship between HR and VIM given as ΔVIM/ΔHR. In previous studies, we have demonstrated that ΔVIM/ΔHR and related biomarkers such as ΔWR/ΔHR are highly correlated with peak $\dot{V}O_2$, and, therefore, could be used as indexes of fitness.[17,24,25]

2.2.5 | Calculating relative fitness—The NHANES estimated $\dot{V}O_2max$ has been used in various studies to gauge the relative fitness of an individual participant. For example, Carnethon et al, who evaluated the relationship between fitness and cardiovascular disease risk factors, calculated age- and sex-specific fitness deciles using the NHANES estimated fitness.[26] Categories of low, moderate, and high fitness were then based on reference standards used for adolescents established by the Fitnessgram program.[27] The Fitnessgram, created by the Cooper Institute, developed sex- and age-specific cardiorespiratory fitness cutoff values for adolescents by a panel of experts.[28] As a use case, we examined the relationships between fitness and cardiovascular disease risk biomarkers (ie, lipid panel levels and BMI percentiles) in NHANES participants, as reported previously.[26] Our alternative approach was to use the values obtained from the NHANES cohort. A linear regression model was applied to evaluate how body mass (weight) affects CPET variables (ΔVIM/ΔHR). The regression line from the normal-BMI subjects was then applied to all participants based on each participant's weight to calculate the percent predicted fitness value (ΔVIM/ΔHR). We then compared the observed to the predicted value as percent predicted and categorized each participant into deciles of the percent predicted value.

2.3 | Statistical analysis

Descriptive statistics are presented with mean and standard deviation (SD). Relationships between fitness variables were assessed using Pearson's correlation. To investigate agreement between the fitness variables (beyond the linear correlation), a matched pairs t test of non-bias and concordance correlation analyses were performed. ΔVIM/ΔHR was calculated for the UCI PERC and NHANES groups, and a one-way ANOVA model was used to compare the slopes (ΔVIM/ΔHR to body mass) between groups. Percent predicted ΔVIM/ΔHR slopes to physical activity variables were also compared using oneway ANOVA models in males and females. Deciles of percent predicted ΔVIM/ΔHR and NHANES estimated $\dot{V}O_2$max values were calculated for males and females. For each of the five outcomes, models were run to examine their functional relationship with each percent predicted decile and NHANES estimated fitness decile. First, a model was performed to assess if the relationship showed a significant deviation from linear, which would suggest either modeling a curvilinear relationship or modeling the fitness deciles as ordinal.[29] In two instances, triglycerides-slope fitness and BMI percentile-NHANES fitness, a deviation from linear was detected and follow-up models were conducted assessing the presence of a quadratic relationship. In both cases, the quadratic relationship was found to be statistically significant and thus was considered the final model. The final model for the remaining outcome-fitness relationships was linear (ie, deciles as continuous) and adjusted for sex, age, and race. To compare the two fitness approaches (percent predicted ΔVIM/ΔHR approach and NHANES estimated $\dot{V}O_2$max) for each of the five outcomes, the Clarke test for comparing competing non-nested models was run.[30] The null hypothesis is that each model provides the same level of fit in predicting the outcomes. Regression models and the Clarke tests were performed using SAS 9.4.

3 | RESULTS

3.1 | Current study (UCI PERC)

Demographics, anthropometrics, and physiological data are presented in Table 1.

3.1.1 | Measured gas exchange and NHANES estimated $\dot{V}O_2$max—

The relationship between the actually measured and NHANES estimated $\dot{V}O_2$max/kg revealed a moderate correlation ($r = 0.53$, 95% CI 0.28, 0.72, $P = 0.001$) (Figure 2A). Measured $\dot{V}O_2$ peak/kg was 8.9 points higher on average than the estimated $\dot{V}O_2$max/kg ($P < 0.001$). The concordance correlation coefficient was 0.33 (95% CI 0.15, 0.50) indicating a low-to-moderate agreement between measured and NHANES estimated $\dot{V}O_2$max/kg. We also found a moderate correlation comparing actual measured $\dot{V}O_2$peak/kg and ΔVIM/ΔHR slopes (from NHANES submaximal protocol) ($r = 0.45$, 95% CI 0.18, 0.66, $P = 0.002$; Figure 2B). To identify possible sources of error in the calculation of the NHANES estimated $\dot{V}O_2$ max/kg, we compared the predicted vs. the measured $\dot{V}O_2$ at NHANES stages 1 and 2, which were significantly different with mean predicted $\dot{V}O_2$ of 19.7 SD ± 4.1 and mean measured $\dot{V}O_2$ of 24.1 SD ± 5.8 for stage 1, and mean predicted $\dot{V}O_2$ of 27.1 SD ± 5.3 and mean measured $\dot{V}O_2$ of 32.5 SD ± 8.1 for stage 2 ($P < 0.01$ for stages 1 and 2; Figure S1). We also found significant differences between the observed HR with mean of 192.8 bpm SD ± 16.3 and predicted peak HR (220 − age) with mean of 204.8 bpm SD ± 1.9 ($P = 0.03$; Figure S1).

3.2 | Existing NHANES Study

3.2.1 | Comparison of ΔVIM/ΔHR: Current study (UCI PERC) and NHANES study—The relationship of ΔVIM/ΔHR slopes to body mass was not significantly different between the current study (UCI PERC) and the NHANES study, $y = 2.03x - 5.33$ with mean slope 112.9 ± 41.6, and $y = 2.36x - 18.14$ with mean slope 118.6 ± 48.6, respectively ($P = 0.70$; Figure S2).

3.2.2 | ΔVIM/ΔHR and physical activity and sedentary time—Percent predicted ΔVIM/ΔHR slope values were compared to physical activity and sedentary time for both males and females as described (Table 2) by Pate et al.[31] Overall, in both males and females, there were significantly higher mean fitness levels in those who reported to be physically active compared to those that were not active, except among males who reported moderate activity. Female participants who reported sedentary time, specifically screen time ≤2 hours daily, had significantly higher predicted fitness levels compared to those with >2 hours of screen time daily ($P < 0.01$), but no difference was seen among male participants ($P = 0.21$).

3.2.3 | ΔVIM/ΔHR and lipid levels—We analyzed a subset of the NHANES participants (2003-2004) with measured lipid panels (n = 740). The lipid levels of the participants were generally within the normal reference ranges, with mean levels ± SD in mg/dL (mean ± SD in mmol/L) as follows: total cholesterol: 185.8 ± 43.7 (4.8 ± 1,1); HDL: 53.4 ± 15.1 (1.4 ± 0.4); triglycerides: 91.1 ± 50.4 (0.95 ± 0.6); and LDL: 88.2 ± 26.9 (2.3 ± 0.7). Nineteen and a half percent of the NHANES participants had high triglyceride levels (>150 mg/dL or 1.69 mmol/L), and 15.1% had low HDL levels (<40 mg/dL or 1.03 mmol/L). Total cholesterol and HDL levels were not significantly different by deciles of percent predicted ΔVIM/ΔHR slopes or NHANES estimated $\dot{V}O_2$max. LDL levels were significantly negatively associated by decile of percent predicted ΔVIM/ΔHR slope ($F = 7.91$, $P < 0.01$) and NHANES estimated $\dot{V}O_2$max ($P < 0.01$; Figure 3B). Triglyceride levels were also significantly negatively correlated by decile of percent predicted ΔVIM/ΔHR slope in a quadratic model ($F_{lin} = 23.29$, $p_{lin} < 0.01$; $F_{quad} = 14.13$, $p_{lin} < 0.01$) and estimated $\dot{V}O_2$max, with a linear relationship ($F = 30.06$, $P < 0.001$; Figure 3C). For each outcome, the percent predicted ΔVIM/ΔHR slope and NHANES estimated $\dot{V}O_2$max final models were compared via the Clarke test as competing non-nested models. The fitness models were not significantly different for total cholesterol ($M_{Clarke} = 19.5$, $P = 0.142$) or triglycerides ($M_{Clarke} = -2.00$, $P = 0.908$). However the percent predicted ΔVIM/ΔHR slope model was a statistically better fit for LDL compared to NHANES ($M_{Clarke} = 32.50$, $P = 0.01$).

3.3 | ΔVIM/ΔHR and BMI percentiles

BMI percentiles were negatively associated by decile of percent predicted ΔVIM/ΔHR slope in a linear model ($F = 44.29$, $P < 0.001$) and estimated $\dot{V}O_2$max in a quadratic relationship ($F_{lin} = 20.79$, $p_{lin} < 0.001$; $F_{quad} = 11.01$, $p_{lin} < 0.01$; Figure 3A). The percent predicted ΔVIM/ΔHR slope and NHANES estimated $\dot{V}O_2$max final models were compared via the Clarke test and not found to be significantly different ($M_{Clarke} = -17.5$, $P = 0.210$).

4 | DISCUSSION

In a prospective study of adolescents, we found that the NHANES estimate of $\dot{V}O_2$max could only account for 28% of the variability of the actually measured $\dot{V}O_2$peak (Figure 2A). Sources of error arose in large measure from the complex equation required to convert HR measured during submaximal exercise to $\dot{V}O_2$max. We found discrepancies between the measured and predicted $\dot{V}O_2$ at the two stages of treadmill exercise, and between the measured and predicted maximal HR (using the formula: 220 beats/min – age). Moreover, in examining the important relationships between LDL and physical fitness in children, which is known to be associated with cardiovascular disease risk,[32] our quantification of physical fitness (using VIM) proved a statistically more robust approach than the NHANES estimate of $\dot{V}O_2$max from submaximal CPET.

Wang et al tested the NHANES treadmill protocol on a small sample of adult men and women (n = 17) and found that the correlation between the estimated $\dot{V}O_2$max and measured $\dot{V}O_2$max/peak was 0.79, greater than what we found in our group of adolescents.[33] To our knowledge, the NHANES estimated $\dot{V}O_2$max protocol has not been validated in a pediatric population and the source of the reference values for the NHANES calculation might also have contributed to the discrepancies between the measured and predicted values. Reference values for the pediatric NHANES estimated $\dot{V}O_2$max were developed from a group of middle-aged NASA employees (9.7% females, mean age 43.7 years in males, 37.6 years in females).[20]

The widely used justification of the use of adult peak VO2 reference values for children was based on the observation that when $\dot{V}O_2$max is scaled to body weight (as ml O_2/min/kg), differences across age-groups seem insignificant. However, $\dot{V}O_2$peak or $\dot{V}O_2$max is correlated significantly higher with lean body mass[34] than with weight because the increase in $\dot{V}O_2$ during exercise results from work performed by skeletal muscle. Body weight reflects metabolically active muscle, but also body fat which is much less active than muscle during exercise. Additionally, the ratio of lean body mass (muscle mass) to body weight is not the same in children and adults.[35] Consequently, great caution should be taken when using $\dot{V}O_2$peak normalized to body weight in adults as reference values for assessing fitness in children.

Since gas exchange was not measured in the NHANES dataset, we could not directly compare our prospectively collected fitness biomarker approaches with the NHANES data. However, we used several approaches to assess the possible utility of our alternative biomarker of fitness (ΔVIM/ΔHR). First, we compared several fundamental relationships in the two datasets. As seen in Figure S2, the regression equation between ΔVIM/ΔHR and body mass in our prospective study cohort was similar to the NHANES dataset .

We then compared ΔVIM/ΔHR with the estimated $\dot{V}O_2$max used in earlier publications to explore the relationship between physical fitness, BMI, and habitual physical activity levels (by recall) in children and adolescents. The work done by each participant in treadmill CPET is a major determinant of HR, and the change in HR was directly measured in the NHANES protocol. Examination of the NHANES $\dot{V}O_2$max algorithm (Figure 1) clearly shows that the $\dot{V}O_2$max estimate is determined in large measure by the change in HR alone. Since both the NHANES algorithm and VIM use the change in HR, we anticipated that there would be broad agreement in the predictive value of the two approaches. As shown in Figure 2, both biomarker approaches showed similar relationships.

Gauging the impact of obesity on CPET in children and adolescents is an area of much-needed research given the interrelationship between obesity and physical fitness[24] and the profound health consequences of childhood obesity across the life span.[36] We compared the relationship of physical fitness to BMI, and circulating lipid levels using ΔVIM/ΔHR and NHANES variables as performed in previous studies.[26] As shown in Figure 3, there were expected, general similarities between the ΔVIM/ΔHR-based fitness percentiles and the NHANES estimated $\dot{V}O_2$max. However, ΔVIM/ΔHR slope revealed a substantially more robust relationship between physical fitness and LDL than the original estimated $\dot{V}O_2$max used in NHANES. This is surprising because in regression analyses, correlations appear to become more robust with an increasing, not decreasing, number of parameters. This effect can result from collinearity and can confound the interpretation of regression results.

Our data suggest that the relationship between HR and work rate alone during submaximal exercise, without the complexity of converting the actually collected data to $\dot{V}O_2$max, might prove to be a valuable biomarker of fitness. Indeed, in the Institute of Medicine Report in 2012[37] focused on fitness assessments in youth, the physical work capacity at a HR of 170 (PWC-170) was cited as a potentially reliable fitness indicator. The relatively weak correlation we found between NHANES estimated $\dot{V}O_2$max and actually measured values does not negate the value of $\dot{V}O_2$max; rather, it should stimulate renewed exploration into which of the systemic responses to exercise are most relevant to health and practical for widespread use.

Biomarkers of fitness are increasingly useful for clinicians and researchers as large-scale efforts are being made to understand the effects of physical activity on health and disease, and to prescribe with precision optimal levels of physical activity in children and across the life span. Biologists from a wide range of disciplines are increasingly attempting to improve accuracy in prediction equations by an overall strategy that minimizes assumptions and other sources of error.[38] For example, these parsimonious approaches are being used to improve predictive testing using advanced analytics, such as machine learning, in a wide range of clinical applications, such as diagnosis of autism[39] and quality of life in patients with Cushing syndrome.[40] Our analysis may accelerate the search for fitness biomarkers that are readily accessible for research and clinical applications targeting exercise therapies in children and adolescents across a wide range of disease and health conditions.

4.1 | Perspective

Weak correlations between estimated and actual $\dot{V}O_2max$ illustrate the importance of exercising caution when using predictions and estimates of $\dot{V}O_2max$ in children as shown in our study. Our findings are consistent with other studies showing the large errors and biases when estimating $\dot{V}O_2max$.[41] We suggest that fitness measurements based on actually measured data may produce more accurate assessments of fitness and, ultimately, better approaches linking exercise to health in children for researchers and clinicians.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Raichlen DA, Pontzer H, Harris JA, et al. Physical activity patterns and biomarkers of cardiovascular disease risk in hunter-gatherers. Am J Hum Biol. 2017;29:e22919.
2. Schmidt MD, Magnussen CG, Rees E, Dwyer T, Venn AJ. Childhood fitness reduces the long-term cardiometabolic risks associated with childhood obesity. Int J Obes. 2016;40: 1134–1140.
3. Freedman DS, Lawman HG, Galuska DA, Goodman AB, Berenson GS. Tracking and variability in childhood levels of BMI: the bogalusa heart study. Obesity. 2018;26:1197–1202. [PubMed: 29888429]
4. Liem RI, Reddy M, Pelligra SA, et al. Reduced fitness and abnormal cardiopulmonary responses to maximal exercise testing in children and young adults with sickle cell anemia. Physiol Rep. 2015;3(4):e12338. [PubMed: 25847915]
5. Sule S, Fontaine K. Abnormal body composition, cardiovascular endurance, and muscle strength in pediatric SLE. Pediatr Rheumatol. 2016;14:50.
6. Cordingley D, Girardin R, Reimer K, et al. Graded aerobic treadmill testing in pediatric sports-related concussion: safety, clinical use, and patient outcomes. J Neurosurg Pediatr. 2016;18:693–702.

7. Shah RV, Murthy VL, Colangelo LA, et al. Association of fitness in young adulthood with survival and cardiovascular risk. JAMA Intern Med. 2016;176:87. [PubMed: 26618471]

8. Ashish N, Bamman MM, Cerny FJ, et al. the clinical translation gap in child health exercise research: a call for disruptive innovation. Clin Transl Sci. 2015;8:67–76. [PubMed: 25109386]

9. Ramsbottom R, Brewer J, Williams C. A progressive shuttle run test to estimate maximal oxygen uptake. Br J Sports Med. 1988;22:141–144. [PubMed: 3228681]

10. Larsen GE, George JD, Alexander JL, Fellingham GW, Aldana SG, Parcell AC. Prediction of maximum oxygen consumption from walking, jogging, or running. Res Q Exerc Sport. 2002;73:66–72. [PubMed: 11926486]

11. Aggarwal R, Ranganathan P. Common pitfalls in statistical analysis: the use of correlation techniques. Perspect Clin Res. 2016;7:187–190. [PubMed: 27843795]

12. Tu Y-K, Maddick IH, Griffiths GS, Gilthorpe MS. Mathematical coupling can undermine the statistical assessment of clinical research: illustration from the treatment of guided tissue regeneration. J Dent. 2004;32:133–142. [PubMed: 14749085]

13. Berlin JA, Antman EM. Advantages and limitations of meta-analytic regressions of clinical trials data. Online J Curr Clin Trials. 1994;3(1):134.

14. Page A, Peeters G, Merom D. Adjustment for physical activity in studies of sedentary behaviour. Emerg Themes Epidemiol. 2015;12(10).

15. Pianosi P, Liem R, McMurray R, Cerny F, Falk B, Kemper H. Pediatric exercise testing: value and implications of peak oxygen uptake. Child (Basel, Switzerland). 2017;4(1):6.

16. Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES 2003–2004): Cardiovascular Fitness Procedures Manual. Bethesda: National Center for Health Statistics; 2004 Accessed at: https://wwwn.cdc.gov/nchs/data/nhanes/2003-2004/manuals/cv_99-04.pdf

17. Bar-Yoseph R, Porszasz J, Radom-Aizik S, Law P, Cooper DM. A novel approach to calculate work rate on a treadmill (TM) in early- and late-pubertal children. Med Sci Sports Exercise. 2017;49:4.

18. Centers for Disease Control and Prevention. 2000 CDC Growth Charts for the United States: Methods and Development. National Center for Health Statistics: 2002. Accessed at https://www.cdc.gov/nchs/data/series/sr_11/sr11_246.pdf

19. Rowland T, Hagenbuch S, Pober D, Garrison A. Exercise tolerance and thermoregulatory responses during cycling in boys and men. Med Sci Sport Exerc. 2008;40:282–287.

20. Jackson AS, Blair SN, Mahar MT, Wier LT, Ross RM, Stuteville JE. Prediction of functional aerobic capacity without exercise testing. Med Sci Sports Exerc. 1990;22:863–870. [PubMed: 2287267]

21. Pate RR, Wang C-Y, Dowda M, Farrell SW, O'Neill JR. Cardiorespiratory fitness levels among US youth 12 to 19 years of age: findings from the 1999–2002 national health and nutrition examination survey. Arch Pediatr Adolesc Med. 2006;160:1005–1012. [PubMed: 17018458]

22. American Academy of Pediatrics. Committee on Public Education. American Academy of Pediatrics: Children, adolescents, and television. Pediatrics. 2001;107:423–426. [PubMed: 11158483]

23. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem. 1972;18:499–502. [PubMed: 4337382]

24. Cooper DM, Leu S-Y, Taylor-Lucas C, Lu K, Galassetti P, Radom-Aizik S. Cardiopulmonary exercise testing in children and adolescents with high body mass index. Pediatr Exerc Sci. 2016;28:98–108. [PubMed: 26730653]

25. Cooper DM, Leu S-Y, Galassetti P, Radom-aizik S. Dynamic interactions of gas exchange, body mass, and progressive exercise in children. Med Sci Sports Exerc. 2014;46(5):877–886. [PubMed: 24091992]

26. Carnethon MR, Gulati M, Greenland P. Prevalence and cardiovascular disease correlates of low cardiorespiratory fitness in adolescents and adults. JAMA. 2005;294:2981–2988. [PubMed: 16414945]

27. Plowman SA, Meredith MD. Fitnessgram/Activitygram Reference Guide. 4th edn. Dallas, TX: The Cooper Institute; 2013.
28. Cureton KJ, Warren GL. Criterion-referenced standards for youth health-related fitness tests: a tutorial. Res Q Exerc Sport. 1990;61:7–19. [PubMed: 2091168]
29. Pasta D Learning when to be discrete: continuous versus categorical predictors. SAS Glob Forum Pap. 2009;248–2009.
30. Clarke KA. ((Department of Political Science U of R. A simple distribution-free test for non-nested model selection. Polit Anal. 2007;15:347–363.
31. Pate RR, Wang C-Y, Dowda M, Farrell SW, O'Neill JR. Cardiorespiratory fitness levels among US youth 12 to 19 years of age. Arch Pediatr Adolesc Med. 2006;160:1005. [PubMed: 17018458]
32. Farrell AW, Finley CE, Grundy SM. Cardiorespiratory fitness, LDL cholesterol, and coronary heart disease (CHD) mortality in men. Med Sci Sport Exerc. 2012;44:2132–2137.
33. Wang C-Y, Haskell WL, Farrell SW, et al. Cardiorespiratory fitness levels among US adults 20–49 years of age: findings from the 1999–2004 national health and nutrition examination survey. Am J Epidemiol. 2010;171:426–435. [PubMed: 20080809]
34. Tompuri T, Lintu N, Savonen K, et al. Measures of cardiorespiratory fitness in relation to measures of body size and composition among children. Clin Physiol Funct Imaging. 2015;35:469–477. [PubMed: 25164157]
35. Kim K, Hong S, Kim EY. Reference values of skeletal muscle mass for korean children and adolescents using data from the Korean National Health And Nutrition Examination Survey 2009–2011. PLoS ONE. 2016;11(4):e0153383. [PubMed: 27073844]
36. Buscot M-J, Thomson RJ, Juonala M, et al. Distinct child-to-adult body mass index trajectories are associated with different levels of adult cardiometabolic risk. Eur Heart J. 2018;39:2263–2270. [PubMed: 29635282]
37. Pate R, Oria M, Pillsbury L. Fitness Measures and Health Outcomes in Youth. Washington, DC: National Academies Press; 2012.
38. Burnham KP, Anderson DR. Data based selection of an appropriate biological model: the key to modern data analytics In: McCullough DR, Barrett RR, eds. Wildlife 2001 London, UK and New York, NY: Elsevier Science; 1992:16–30.
39. Levy S, Duda M, Haber N, Wall DP. Sparsifying machine learning models identify stable subsets of predictive features for behavioral detection of autism. Mol Autism. 2017;8:65. [PubMed: 29270283]
40. Roset M, Badia X, Forsythe A, Webb SM. Mapping CushingQol scores onto SF-6D utility values in patients with Cushing’s syndrome. Patient. 2013;6:103–111. [PubMed: 23549927]
41. Aadland E, Andersen LB, Lerum Ø, Resaland GK. The Andersen aerobic fitness test: new peak oxygen consumption prediction equations in 10 and 16-year olds. Scand J Med Sci Sports. 2018;28:862–872. [PubMed: 28940675]

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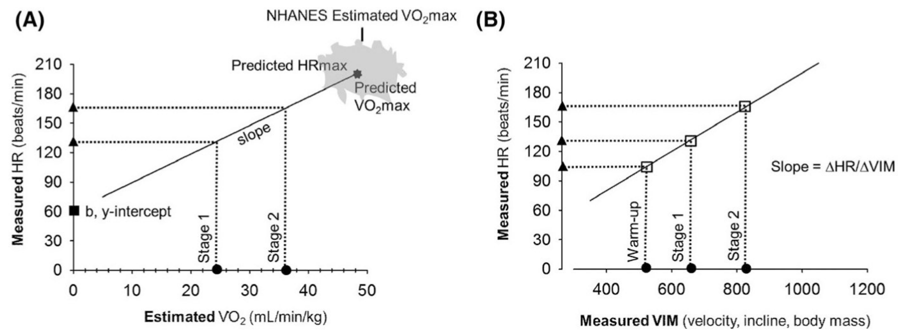

FIGURE 1.

Two approaches to fitness. A, Elements of the NHANES calculation of fitness as estimated $\dot{V}O_2$max in ml/min/kg. The calculation assumes a linear relationship between HR and $\dot{V}O_2$ during exercise. Predicted HRmax and predicted $\dot{V}O_2$max were necessary for the protocols. The resulting estimated $\dot{V}O_2$max (likely found somewhere in the gray area) differs from the predicted values. See text for additional descriptions. B, Elements of a new analysis of NHANES data to determine fitness. We have shown that a combination of the measured VIM variables (treadmill velocity and treadmill incline) and body mass is linearly related to work rate. We used the slope of the HR-VIM relationship (determined by linear regression) from the NHANES HR data at warm-up, stage 1, and stage 2 as a fitness variable

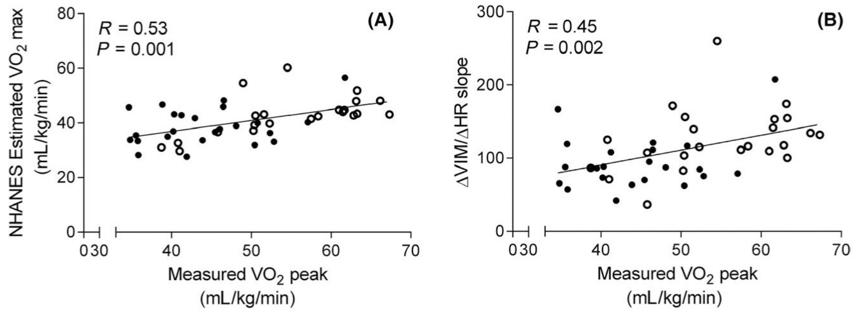

FIGURE 2.

Relationships between measured and estimated fitness variables (n = 53 adolescents). A, A comparison between NHANES estimated $\dot{V}O_2$max and actual $\dot{V}O_2$peak. B, A comparison between measured $\dot{V}O_2$peak and ΔVIM/ΔHR slopes. Closed circles represent individual female subjects, open circles represent individual male subjects, and solid line represents linear regression of NHANES estimated $\dot{V}O_2$max and measured $\dot{V}O_2$peak

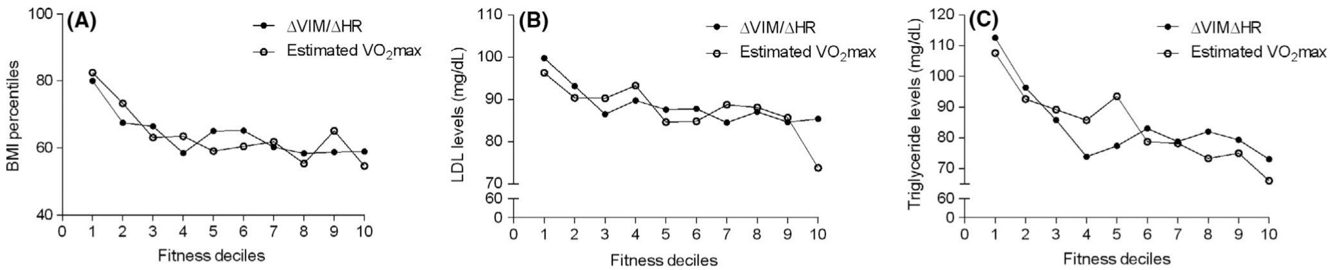

FIGURE 3.

BMI percentiles (A) and LDL (B) and triglyceride (C) levels by deciles of fitness. Closed circles represent mean ΔVIMΔ/HR percent predicted fitness, and open circles represent mean NHANES estimated $\dot{V}O_2max$

TABLE 1

Demographic characteristics of study participants

	Current study N = 53	**NHANES study n = 4508**
Age, mean (SD)	15.8 (1.8)	15.0 (2.0)
Sex, n (%)		
Males	27 (51)	2305 (51.1)
Females	26 (49)	2203 (48.9)
Race, n (%)		
Black	0	1382 (30.7)
Hispanics	3 (6)	1812 (40.2)
Other	19 (36)	177 (3.9)
White	31 (58)	1137 (25.2)
BMI categories, n (%)		
Under (<5th percentile)	0	115 (2.6)
Normal (5th-<85th percentile)	46 (87)	2828 (62.9)
Over (85th-<95th percentile)	6 (11)	745 (16.6)
Obese (≥95th percentile)	1 (2)	810 (18.0)
$\dot{V}O_2$max, estimated mean (SD)		
Males	41.3 (7.7)	46.1 (9.4)
Females	39.4 (6.6)	39.0 (8.6)
$\dot{V}O_2$peak, measured mean (SD)		
Males	53.0 (9.7)	
Females	45.1 (7.1)	

TABLE 2

Fitness, physical activity, and sedentary time for males and females

	Males			Females			
	N	**Mean (SD)**	***P* value**	**N**	**Mean (SD)**	***P* value**	**Agreement with pate**
Vigorous activity, past 30 d							
Yes	1798	96.7 (32.4)	<0.01	1350	101.7 (38.2)	<0.01	Yes[a]
No	466	91.5 (29.7)		816	93.6 (32.4)		
Moderate activity, past 30 d							
Yes	1397	96.2 (31.3)	0.24	1409	99.7 (37.1)	0.08	Yes[a]
No	864	94.6 (32.9)		757	96.7 (35.0)		
Compared with others							
More active	785	100.4(29.8)	<0.01	609	106.3 (39.5)	<0.01	Yes[a]
About the same	214	84.0 (32.8)		362	90.5 (30.9)		
Less active	1260	94.6 (32.5)		1194	97.2 (35.5)		
Sedentary time							
≤2 h	805	96.6 (31.9)	0.21	839	101.4 (36.5)	<0.01	Yes[a]
>2 h	1500	94.9 (31.7)		1364	97.0 (36.1)		

Note: Fitness refers to percent predicted fitness using ΔVIM/ΔHR slopes.

P values refer to sex-specific comparisons within each activity category using one-way analysis of variance.

Sedentary time refers to time spent sitting and watching television, videos, or computers.

[a]Agreement for both males and females in reference to Pate et al.[31]. Pate et al used a cutoff of ≥3 h for sedentary time.